



Express Mail Certificate EV 367 776 236 US

PTO/SB/08a (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL  
INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 1 of 1

**Complete if Known**

Application Number	10/611,741
Filing Date	July 1, 2003
First Named Inventor	Adnan M.M. Mjalli, et al.
Art Unit	1616
Examiner Name	Barbara P. Badio, Ph.D.
Attorney Docket Number	41305-287124

U.S. PATENT DOCUMENTS					
Examiner Initials *	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code <sup>2</sup> (if known)			
BB	1	US - 5,922,770	7/13/1999	Peschke, et al.	Col.94, line 20-35
		US-			
		US-			
		US-			
		US-			

FOREIGN PATENT DOCUMENTS						
Examiner Initials *	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>3</sup>
		Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>

Examiner Signature	Badio	Date Considered	1/7/05
-----------------------	-------	--------------------	--------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Please type a plus sign (+) inside this box → +

PTO/SB/08A (09-00)

Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449APTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>		<b>Complete If Known</b>	
		Application Number	Div. App. of 09/799,317
		Filing Date	Herewith
		First Named Inventor	Adnan M.M. Mjalli
		Group Art Unit	1616
		Examiner Name	Barbara P. Badio
		Attorney Docket Number	41305-287142
Sheet 1 of 4		Express Mail Certificate	EV 127 540 449 US

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
BB	1	4,166,452		Generales, Jr.	09-04-79	
	2	4,265,874		Bonsen, et al.	05-05-81	
	3	4,356,108		Schwab, et al.	10-26-82	
	4	4,873,313		Crawford, et al.	10-10-89	
	5	4,963,539		Delaney	10-16-90	
	6	5,202,424		Vlassara, et al.	04-13-93	
	7	5,585,344		Vlassara, et al.	12-17-96	
	8	5,688,653		Ulrich, et al.	11-18-97	
	9	5,864,018		Morser, et al.	01-26-99	
	10	5,939,526		Gaugler, et al.	08-17-99	
BB	11	6,100,098		Newkirk	08-08-00	

FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>3</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)				
BB	12	WO	00/20458		The Trustees of Columbia University in NYC	04-13-00		✓
	13	WO	00/20621		The Trustees of Columbia University in NYC	04-13-00		✓
	14	WO	97/26913		The Trustees of Columbia University in NYC	07-31-97		✓
	15	WO	97/39121		Schering Aktiengesellschaft	10-23-97		✓
	16	WO	9739125		Schering Aktiengesellschaft	10-23-97		✓
	17	WO	98/22138		The Trustees of Columbia University in NYC	05-28-98		✓
	18	WO	99/07402		The Trustees of Columbia University in NYC	02-18-99		✓
	19	WO	99/18987		The Trustees of Columbia University in NYC	04-22-99		✓
	20	WO	99/54485		The Trustees of Columbia University in NYC	10-28-99		✓
	21	WO	95/09838		Merrell Dow Pharmaceuticals Inc.	04-13-95		✓
BB	22	WO	95/35279		Merrell Pharmaceuticals Inc.	12-28-95		✓
	23	WO	97/22618		Vertex Pharma- ceuticals Incorporated	06-26-97		✓
	24	WO	96/32385		Hoechst Marion Roussel Inc.	10-17-96		✓

Please type a plus sign (+) inside this box → +

PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449APTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Complete if Known	
		Application Number	Div. App. of 09/799,317
		Filing Date	Herewith
		First Named Inventor	Adnan M.M. Mjalli
		Group Art Unit	1616
		Examiner Name	Barbara P. Badio
		Attorney Docket Number	41305-287142
		Express Mail Certificate	EV 127 540 449 US
Sheet	2	of	4

BB	25	WO	99/50230	Vertex Pharma- ceuticals Incorporated	10-07-99	✓
	26	GB	2 005 674	Carlo Erba S.p.A.	04-25-79	✓
	27	WO	98/33492	Fox Chase Cancer Center	08-06-98	✓
BB	28	WO	99/25690	University of Kansas Medical Center	05-27-99	✓

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	Cite No.†	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>	
BB	29	Albercio, F. & Carpino, L.A., "Coupling Reagents and Activation" <i>Methods in Enzymology</i> 289:104-126, Academic Press, San Diego (1997)	✓	
	30	Barton, J.W., "In Protection of N-H Bonds and NR <sub>3</sub> " <i>Protective Groups in Organic Chemistry</i> , J.F.W. McOmie, ED., Plenum Press, New York, NY (1973)	✓	
	31	Berge, S.M., et al., "Pharmaceutical Salts" <i>Journal of Pharmaceutical Sciences</i> 66:1-19 (1977)	✓	
	32	Chitaley, K., et al., "Antagonism of Rho-Kinase Stimulates Rate Penile Erection via a Nitric Oxide-Independent Pathway" <i>Nature Medicine</i> 7:119-122 (2002)	✓	
	33	Degenhardt, T.P., et al., "Chemical Modification of Proteins by Methylglyoxal" <i>Cell Mol. Biol.</i> , 44:1139-1145 (1998)	✓	
	34	Dyer, D.G., et al., "Accumulation of Maillard Reaction Products in Skin Collagen in Diabetes and Aging" <i>J. Clin. Invest.</i> , 91:2463-2469 (1993)	✓	
	35	Dyer, D.G., et al., "Formation of Pentosidine during Nonenzymatic Browning of Proteins by Glucose" <i>J. Biol. Chem.</i> , 266:11654-11660 (1991)	✓	
	36	Greene, T.W., "Protection for the Amino Group" <i>Protective Groups in Organic Synthesis</i> , John Wiley and Sons, New York, NY, Chapter 7 (1981)	✓	
	37	Hammes, H.P., et al., "Diabetic Retinopathy Risk Correlates with Intracellular Concentrations of the Glycoxidation Product N <sup>ε</sup> -(Carboxymethyl) Lysine Independently of Glycohaemoglobin Concentrations" <i>Diabetologia</i> , 42:603-607 (1999)	✓	
	38	Hoffman, M.A., et al., "RAGE Mediates a Novel Proinflammatory Axis: A Central Cell Surface Receptor for S100/Calgranulin Polypeptides" <i>Cell</i> , 97:889-901 (1999)	✓	
	39	Hori, O., et al., "The Receptor for Advanced Glycation End Products (RAGE) Is a Cellular Binding site for Amphoterin" <i>J. Biol. Chem.</i> , 270:25752-761 (1995)	✓	
	40	Huttunen, H.J., et al., "Receptor for Advanced Glycation End Products (RAGE)-Mediated Neurite Outgrowth and Activation of NF-Kappa B Require the Cytoplasmic Domain of the Receptor But Different Downstream Signaling Pathways" <i>J. Biol. Chem.</i> 274(28):19919-24 (1999)	✓	
BB	41	Kumar, S.R., et al., "RAGE at the Blood-Brain Barrier Mediates Neurovascular Dysfunction Caused by Amyloidβ <sub>1-40</sub> Peptide" <i>Neurosci. Program</i> , 141-#255.19 (2000)	✓	

Substitute for form 1449APTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 3 of 4**Complete if Known**

Application Number	Div. App. of 09/799,317
Filing Date	Herewith
First Named Inventor	Adnan M.M. Mjallil
Group Art Unit	1616
Examiner Name	Barbara P. Badio
Attorney Docket Number	41305-287142
Express Mail Certificate	EV 127 540 449 US

BB	42	Leder, A. et al., "v-HA-ras Transgene Abrogates the Initiation Step in Mouse Skin Tumorigenesis: Effects of Phorbol Esters and Retinoic Acid" <i>Proc. Natl. Acad. Sci., USA</i> , 87:9178-9182 (1990)	✓
	43	Li, J. et al., "Sp1-Binding elements in the Promoter of RAG Are Essential for Amphoterin-Mediated Gene Expression in Cultured Neuroblastoma Cells." <i>J. Biol. Chem.</i> , 273:30870-30878 (1998)	✓
	44	Li, J. et al., "Characterization and Functional Analysis of the Promoter of RAGE, the Receptor for Advanced Glycation End Products," <i>J. Biol. Chem.</i> , 272:16498-16506 (1997)	
	45	Lugering, N. et al., "The Myeloid Related Protein MRP8/14 (27E10 Antigen)—Usefulness as a Potential Marker for Disease Activity in Ulcerative Colitis and Putative Biological Function" <i>Eur. J. Clin. Invest.</i> , 25:659-664 (1995)	✓
	46	Miyata, T. et al., "β <sub>2</sub> -Microglobulin Modified with Advanced Glycation End Products Is a Major Component of Hemodialysis-Associated Amyloidosis" <i>J. Clin. Invest.</i> , 92:1243-1252 (1993)	✓
	47	Miyata, T. et al., "The Receptor for Advanced Glycation End Products (RAGE) Is a Central Mediator of the Interaction of AGE-β <sub>2</sub> Microglobulin with Human Mononuclear Phagocytes Via an Oxidant-Sensitive Pathway" <i>J. Clin. Invest.</i> , 98:1088-1094 (1996)	✓
	48	Neeper, M., et al., "Cloning and Expression of a Cell Surface Receptor for Advanced Glycosylation End Products of Proteins" <i>J. Biol. Chem.</i> , 267:14998-15004 (1992)	✓
	49	Parkkinen, J. et al., "Amphoterin, the 30-kDa Protein in a Family of HMG1-Type Polypeptides" <i>J. Biol. Chem.</i> , 268:19726-19738 (1993)	✓
	50	Rammes, A. et al., "Myeloid-Related Protein (MRP) 8 and MRP 14, Calcium-Binding Proteins of the S100 Family, Are Secreted by Activated Monocytes via a Novel, Tubulin-Dependent Pathway" <i>J. Biol. Chem.</i> , 272:9496-9502 (1997)	✓
	51	Rauvala, H. et al., "Isolation and Some Characteristics of an Adhesive Factor of Brain That Enhances Neurite Outgrowth in Central Neurons" <i>J. Biol. Chem.</i> , 262:16625-16635 (1987)	✓
	52	Reddy, S. et al., "N <sup>ε</sup> -(Carboxymethyl) Lysine Is a Dominant Advanced Glycation End Product (AGE) Antigen in Tissue Proteins" <i>Biochem.</i> , 34:10872-10878 (1995)	✓
	53	Schafer, B.W., et al., "The S100 Family of EF-Hand Calcium-Binding Proteins: Functions and Pathology" <i>TIBS</i> , 21:134-140 (1996)	✓
	54	Schleicher, E.D., et al., "Increased Accumulation of the Glycoxidation Product N <sup>ε</sup> -(Carboxymethyl) Lysine in Human Tissues in Diabetes and Aging" <i>J. Clin. Invest.</i> , 99(3):457-468 (1997)	✓
	55	Schmidt, A.M. et al., "The Dark Side of Glucose" <i>Nature Med.</i> , 1:1002-1004 (1995)	✓
	56	Schmidt, A.M., et al., "The V-Domain of Receptor for Advanced Glycation Endproducts (RAGE) Mediates Binding of AGEs: A Novel Target for Therapy of Diabetic Complications:" <i>Supplement to Circulation</i> Vol. 96, #194 (1997)	✓
BB	57	Taguchi, A. et al., "Blockade of RAGE—Amphoterin Signalling Suppresses Tumour	✓

Please type a plus sign (+) inside this box 

PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449APTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		<b>Complete if Known</b>	
		Application Number	Div. App. of 09/799,317
		Filing Date	Herewith
		First Named Inventor	Adnan M.M. Mjalli
		Group Art Unit	1616
		Examiner Name	Barbara P. Badio
Sheet <u>4</u> of <u>4</u>		Attorney Docket Number <u>41305-287142</u> Express Mail Certificate <u>EV 127 540 449 US</u>	

		Growth and Metastases" <i>Nature</i> , 405:354-360 (2000)	
BB	58	Tanaka, N., et al., "The Receptor for Advanced Glycation End Products Is Induced by the Glycation Products Themselves and Tumor Necrosis Factor- $\alpha$ through Nuclear Factor- $\kappa$ B, and by 17 $\beta$ -Estradiol through Sp-1 in Human Vascular Endothelial Cells" <i>J. Biol. Chem.</i> , 275:25781-25790 (2000)	✓
	59	Teillet et al., "Food Restriction Prevents Advanced Glycation End Product Accumulation and Retards Kidney Aging in Lean Rats" <i>J. Am. Soc. Nephrol.</i> , 11:1488-1497 (2000)	✓
	60	Vlassara, H., "Advanced Glycation End-Products and Atherosclerosis" <i>The Finnish Medical Society DUODECIM, Ann. Med.</i> , 28:419-426 (1996)	✓
	61	Wautier et al., "Receptor-Mediated Endothelial Cell Dysfunction in Diabetic Vasculopathy: Soluble Receptor for Advanced Glycation End Products Blocks Hyperpermeability in Diabetic Rats" <i>J. Clin. Invest.</i> , 97:238-243 (1996)	✓
	62	Yan, S.-D., et al., "RAGE and Amyloid- $\beta$ Peptide Neurotoxicity in Alzheimer's Disease" <i>Nature</i> 382:685-691 (1996)	✓
	63	Yan, S.-D., et al., "An Intracellular Protein That Binds Amyloid- $\beta$ Peptide and Mediates Neurotoxicity in Alzheimer's Disease" <i>Nature</i> , 389:689-695, (1997)	✓
	64	Yan, S.-D. et al., "Amyloid- $\beta$ Peptide—Receptor for Advanced Glycation Endproduct Interaction Elicits Neuronal Expression of Macrophage-Colony Stimulating Factor: A Proinflammatory Pathway in Alzheimer Disease" <i>Proc. Natl. Acad. Sci., USA</i> , 94:5296-5301 (1997)	✓
	65	Yan, S.-D. et al., "Receptor-Dependent Cell Stress and Amyloid Accumulation in Systemic Amyloidosis" <i>Nat. Med.</i> 6:643-651 (2000)	✓
	66	Yan, S.-D. et al., "Enhanced Cellular Oxidant Stress by the Interaction of Advanced Glycation Endproducts With Their Receptors Binding Proteins" <i>J. Biol. Chem.</i> 269:9889-9897 (1994)	✓
	67	Zimmer, D. et al., "The S100 Protein Family: History, Function, and Expression" <i>Brain Res. Bull.</i> , 37:417-429 (1995)	✓
BB	68	International Search Report for PCT/US 01/17251 dated 8/14/01	

Examiner Signature	<u>Badio</u>	Date Considered	<u>1/7/05</u>
--------------------	--------------	-----------------	---------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

**Burden Hour Statement:** This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.**  
41305-287124 WINLIB01:1014665